

Non-technical Abstract**A Phase I Study of Vaccination with Lethally Irradiated, Autologous Acute Myeloblastic Leukemia Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor**

No consistently effective therapy exists for advanced myelodysplasia or acute myelogenous leukemia (AML). Recent studies have demonstrated that targets present on many AML cells can elicit T cell and antibody responses in some patients. We have conducted extensive laboratory studies using a new strategy for augmenting anti-tumor immune responses in murine systems. By inserting the immunostimulatory gene granulocyte-macrophage colony stimulating factor (GM-CSF) into mouse tumor cells and injecting them under the skin, systemic anti-tumor immune responses have been induced, resulting in the eradication of implanted tumors at distant sites. Importantly, the tumor vaccine cells could be lethally irradiated after genetic engineering without compromising the efficacy of treatment. These effects have been observed in multiple murine tumors including acute leukemia, melanoma, renal cell carcinoma, prostate carcinoma, colon carcinoma, bladder carcinoma, sarcoma, neuroblastoma, glioma, and lymphoma.

Based on these studies, we have performed during the past five years three Phase I studies in patients with metastatic melanoma or metastatic nonsmall lung carcinoma of vaccination with lethally irradiated, autologous tumor cells engineered by viral mediated gene transfer to secrete GM-CSF. These studies have documented the consistent induction of potent anti-tumor immunity (associated with clinical benefit in a significant number of patients) without the development of significant toxicity. In the proposed study, we will attempt to extend these principles to advanced myelodysplasia or AML. In this trial, harvested myeloblasts will be prepared to single cell suspension, infected with an adenovirus expressing human GM-CSF, irradiated, and frozen.

The proposed study seeks to determine the safety and toxicity of administering this type of genetically engineered cancer vaccine. While the study is not intended to assess the efficacy of this treatment, it will provide important information that will be incorporated into future efficacy studies. Measurements will be made in this trial of any immunologic responses stimulated by the vaccine.